V. EXAMINATIONS OF STOMACH CONTENTS.

Lectures and demonstrations, together with practical exercises, are held daily. The material from the different clinics is used and is supplemented whenever necessary by material kept ready for the various exercises. Every student is assigned some special subject on which he looks up the literature and prepares a short essay giving the literature and the results of his personal investigations, together with specimens to substantiate his views. The best of these are read and discussed before the class.

Daily conferences are held and individual efficiency ascertained by private quizzes. A laboratory note book is kept by each student containing the lectures and personal observations on all material submitted for examination. At the end of the course a written examination and a practical examination in laboratory diagnosis covering the different subjects taught, are given.

PERNICIOUS MALARIA.*

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In the widest sense, pernicious malaria is one which threatens life. It is malaria characterized by severe obstinately recurring fever, pronounced intractable anaemia, pernicious visceral symptoms, frequently with abortive paroxysms without chills, considerable depression, tendency to recurrence and the presence in the blood of the aestivo-autumnal form (or forms, as some will have it) of the plasmodium malariae.

Pernicious malaria constitutes but a small proportion of cases of aestivo-autumnal malaria, yet a few pernicious cases have occurred from infection with the ordinarily benign tertian parasite (Ziemann, French and one of our own observation).

The causal factor is the aestivo-autumnal parasite, whose fuller description falls to Drs. Wells and Preble,—a plasmodium called aestivo-autumnal to contrast it with the milder vernal organisms, a small, round endoglobular parasite, at first unpigmented, one-eighth to one-

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fifth of the size of a red cell, annular in form when resting, but often assuming various shapes in its amoeboid movements, becoming less mobile though more pigmented as it grows, till at maturity it is round, though always relatively small, contains a centrally located mass of pigment, fills the shrunken deformed "Brassy" red corpuscles, sporulates in the internal organs and eventuates in the crescent form when the infection has lasted some time.

Pathogeneses of Pernicious Symptoms.

Melanosis of the brain and other organs, early noted by Plehn and Frerichs, is observed in other diseases and does not adequately explain perniciousness. Laveran explained it by plasmodial thrombosis, Kelsch and Kiener by endothelial changes, but the leading role is played by the red blood cells, whose loss of elasticity and irregular contour keep them from passing the lumen of the visceral capillaries with their usual facility, hence the blood current is slowed. As additional evidence of this fact, only the normal red cells escape from the vessels in case of capillary hemorrhages, while the infected parasite-laden red corpuscles always remain in the vessels.

Regressional, sometimes extensive, organic changes result in the organ involved, the cerebrum, the crura cerebri, medulla, gastro-intestinal mucosa, spleen, liver, kidney, etc. Of wholly secondary importance are the purely pigmentary phagocytic or parasitic thromboses.

Secondary elements in determination of perniciousness are:

One. Individual factors, as arterio-sclerosis, renal disease, cardiac changes (right ventricular dilatation from fever or toxaemia), alcoholism, insolation, overwork, malnutrition, lack of acclimation, etc.

Two. The character of the parasites.

Three. Their great number, their abundance at least in the internal parts. Parasites of the aestivo-autumnal group in the blood with large blocks of central pigment usually indicate many plasmodia in the viscera.

The parasites are often few in the peripheral blood or indeed in the blood of a splenic puncture and still found in simply enormous numbers in the brain at autopsy (Bastianelli, Marchiafara and Bignami).

Four. Greater activity in multiplication, even in the peripheral blood where they are usually less abundant in the sporulating stage. Several plasmodia are sometimes found in a single corpuscle and the spores may number 10, 20, even 30.

Five. Increased toxicity of the malarial parasites has been invoked, but this theory is purely assumptive as the malarial toxine is yet to be isolated, still necroses in the spleen, liver and kidney and the great morphologic alteration on the brassy red corpuscles are quite consistent with the hypothesis of increased toxicity producing pernicious symptoms.

SYMPTOMATOLOGY.

A. Fever. Malaria should not be classified according to the clinical characters of the fever, since double or triple infections, mixed infections, or several rudimentary generations of parasites may exist and on the other hand fever may be lacking in the severer forms. No absolute dependence should be placed upon the classic division by Lorain of the paroxysm into chill, fever, and sweating inasmuch as the chill may be absent. The anamnesis is quite unreliable in the more pernicious forms.

In the tertian type of aestivo-autumnal intermittent fever, the temperature rises as high as 104 deg, with a paroxysm lasting 24 to 36 (48) hours. The curve often shows a period of invasion, a fastigium, pseudocrisis, precritical perturbation and genuine crisis, although many atypical, procrastinating, anticipating, duplicating, oscillating varieties are seen.

The paroxysm is often rudimentary, there is severe headache, pronounced alimentary symptoms, difficult respirations and great nervousness. The blood reveals sometimes delayed, sometimes precocious pigment in the small parasites, again no plasmodia are found the first few days, crescents appear in a week or so, sometimes developing early, seemingly under the favoring influence of quinine or at other times early cinchinozation may wholly inhibit their development.

The quotidian type of aestivo-autumnal intermittent is produced by the same parasite. The individual paroxysms are short, 6 to 8 hours, there is usually but one abrupt febrile movement without any special oscillations after which the temperature is frequently subnormal, 95 deg. The fever soon loses its regularity. A tendency to anticipation or procrastination of the attack frequently denotes the gravity of the infection. The symptoms are usually milder and less typical than in the tertian autumnal intermittent and spontaneous recovery is not infrequent. In contradistinction to these two types of more or less regular evolution, stands an irregular autumnal variety, designated as irregular or subcontinuous, a better term than continuous or remit-

tent. It may be mild or grave, is characterized by headache, prostration, pains in the back and legs, digestive symptoms, restlessness, delirium, a rapid and often dirotic pulse, liver and spleen enlargement, febrile urine, dilated right heart and one or several generations of plasmodia in the blood.

B. Splenic tumor is rarely lacking (Laveran), although Plehn, Kelsch and Kiener record its absence. As in typhoid there is some disparity between the clinical and the pathological findings. While rarely failing us on the post mortem table, conditions during life, such as pain, meteorism, etc., favor its detection by palpation in 88 per cent only. In numbers of malaria cases, benign and malignant, we have failed to feel the spleen, where the blood examination determined the diagnosis. In one comatose case with no physical findings other than a hard easily palpable spleen the hardness of the organ pointed to a chronic recurrent malaria and the diagnosis was amply established by the plasmodia in the blood. In this case, recovery ensued upon hypodermatic injections of quinine. This case was observed by me while interne in Cook County Hospital, and is the first instance of pernicious malaria observed in that institution, at least.

In another pernicious case, a boy with convulsions and coma, without history or other significant signs, the hard rather large spleen suggested a malarial origin and the diagnosis was conformed by careful blood examination made by Dr. A. F. Lemke, then house physician. We observed this case from its incipiency and it was later published by Dr. J. B. Herrick (Journal Amer. Med. Assn., May 2, 1896,) together with a similar convulsive case seen by him in consultation practice.

The ordinary tertian parasite was found.

C. The blood (exclusive of the plasmodium).

Anaemia is usually very pronounced in pernicious malaria. Indeed the first paroxysm of the ordinary malaria may reduce the red corpuscles one-half to one million cells. It may resemble pernicious anaemia (in children, Fayrer, Ewart or in pregnancy). Kelsch records an instance where the red cells were but 500,000 to the mm.

Leucopenia of 1,000 to 2,000 white cells to the mm. is the rule, yet leucocytosis occurs in complications, as pneumonia or purulent accident and in uncomplicated pernicious types, as the tropical black water fever. Here usually the leucocyte increase is a lymphocytosis.

D. Circulation. The pulse as in benign malaria is often slow and dicrobic at first with close resemblance to the typhoid pulse, while it later becomes fast and weak. Right ventricular dilatation is frequent. The coincidence of malaria with ulcerative endocarditis, first reported by Duroziez and Lancereaux, is now rather generally denied, yet one case of our own came to autopsy where clinically the signs of malignant endocarditis and plasmodia in the blood, coexisted. Deep melanosis especially of the liver and spleen were found.

E. Respiratory System. Malaria cannot produce pneumonia which must be regarded as a secondary infection, since malaria per se has no phlogogenic power (Baccelli). Plasmodia have, however, been seen in the sputum. Transient somewhat migratory pulmonary congestions occur.

F. Digestive Tract. Intestinal symptoms, with haematemesis, bilious vomiting and cardralgia, observed in the severer forms of malaria, are meteorism, constipation or more rarely diarrhoea, which may be choleraic in character. Infarction of the intestinal blood vessels with plasmodia explain the bowel symptoms (Barker, Dock, Marchiafava and Bignami). Intestinal hemmorrhage, noted by Bolin and Frerichs, is rare. Torti spoke of a perniciosa dysenterica, which now-a-days is seen especially in Madagascar. In this connection a case seen in St. Luke's Hospital this fall and presented in clinic, is of special interest. A man with typhoid fever curve, dicrotic pulse, diazo reaction and enlarged spleen, complained of severe diarrhoea and later of profuse bloody bowel movements. There was no Widal reaction roseolae nor mental apathy. The blood examination revealed crescents and with them annular intra corpuscular somewhat pigmented aestivo-autumnal plasmodia, whose rather rare coincidence was interpreted as indicating a severe malarial infection. Prompt and heavy administration of quinine abolished temperature, diarrhoea and dysentery and, persisted in, prevented recurrence. No amoebae coli were found in the dejections. Icterus from sepis, polycholia, etc., is frequent in the pernicious cases. The occasional acute ascites is explained by pyle thrombosis or acute plugging of the portal capillaries with melainferous cells.

G. Renal System. We will not encroach upon the urinary findings assigned to Dr. Wells more than to briefly cite a case of diabetes insipidus seen with Dr. Van Hoosen in a patient in whose blood plasmodia were at one time seen by Drs. Cooke and Preble. The diabetes

persisted after all blood phenomena had disappeared (Dr. Stanley P. Black of Pasadena).

In an advanced interstitial nephritis with weak heart and uraemia observed in my Cook County Hospital service Sept.-Oct., 1897, terbian malarial parasites were found in moderate numbers. The fatal factor was not determined as an autopsy could not be secured. The Italian observers recognize nephritis as an important factor in the determination of perniciousness.

H. Nervous System. Severe malaria exerts an almost selective action on the nervous system, indeed the older writers like Van Swieten called malaria a neurosis. There is scarcely a nervous symptom, says Mannaberg which is not occasionally observed in malaria. We may see convulsions, as in Dr. Herrick's two cases, minor spasm, all degrees of involvment of the sensorium from simple depression to mania or coma, tremors, choreic tetanic or athetotic movements, contractures, aphasia, cerebral bulbar spinal or peripheral paralysis, pseudosclerosis, pseudotabes, paralysis agitans or Landry's paralysis.

It is often difficult from a clinical standpoint to decide how great a role is played by the intoxication per se or how far the findings are explained by organic changes, as capillary hemorrhages, thrombosis, capillary plugging with parasite laden erythrocytes, the more direct and usual explanation. In another comatose case the parasites were so abundant that they could be obtained in enormous numbers from any capillary in the body at the autopsy (unpublished case of Dr. J. B. Herrick). There were no focal lesions such as have just been reported by Spiller of Philadelphia (Amer. Jour. Med. Sci., Dec., 1900).

The perniciosa comatosa is the most frequent of all cerebral types. Still another comatose case has been observed in Dr. Herrick's County Hospital service in Oct.-Nov., of this year.

It is bound to no type of fever, the coma may intermit or at some phase be associated with delirium or convulsions. This class is due to the aestivo-autumnal parasite or the "second group" of Mannaberg, including three species of parasites. Mannaberg states that only two cases (those of French and Zehmann) are known where the ordinary tertian plasmodium occurred, to which can be certainly added one at least of our own observation.

Before death the fever may be very high or subnormal. The pulse remains regular and slow until death approaches, when it becomes soft, thready and rapid. Respiration varies from quiet and regular to

noisy or of the Cheyne-Stokes quality. Death is usually cardiac after a protracted struggle, with pronounced dilation of the right heart, hemorrhages, petechial and retinal, etc. Pernicious cerebral forms may closely simulate meningitis, with slow pulse, headache, rigidity and tenderness of neck and spine, hyperaesthesia, with deeping sopor, convulsions, involuntaries arrlythmia and final coma or may again resemble acute bulbar palsy, etc.

I have never observed in Chicago the pernicious algid syncopal, cardialgic, haemoglobinuric, choleraic or biliary types seen personally in cases originating in the Roman campagna, except in one instance of recurrrent chagris fever in a physician on the high way to recovery where there had been haemoglobinuria and at the time of examination there was marked ieterus, polycholic stools, tender enlarged spleen, remittent temperature and crescents following the disappearance of the fever of a small pigmented parasite.

Great care is imperative in the diagnosis of pernicious chronic malaria and malarial cachexia of which latter the leading findings are anaemia, hydraemia, pigmentary deposits and visceral changes, enlargement of the liver and spleen, etc. With negative blood findings, the diagnosis should be held in suspense, though quinine should be administered in cases of doubt. Most often later developments disclose sepsis, malignant disease, etc., as in the case of an Italian observed two months ago in the County Hospital who had temperature, an enlarged liver and spleen. Sudden icterus just before death, heavy Cucocytosis, a history of malaria but no plasmodia and no Widal test. No diagnosis was made and the autopsy showed a melanosarcoma of the dura with metastases.

Diagnosis and Differentiation.

In the diagnosis, the locality, history of prevous infection we may prove suggestive.

One. The finding of the aestivo-autumnal parasite, discussed in this symposium by Dr. Wells and Preble is the ultimate test. The detection of the younger forms of this type demands considerable experience, while the ordinary tertian and quartan plasmodie are much more easily determined even by younger students.

The young motile annular non-pigmented parasites are readily mistaken for vaeuoles or irregularities in the protoplasm of the red blood cells and conversely vaceuoles, etc., in the red corpuscles must not be

confused with mechanic or chemic changes in the otherwise normal red cells.

The first examination may give negative results yet much pigment or red corpuscles in the leucocytes is somewhat significant. Even the first slide may demonstrate many plasmodia, and the diagnosis is simple when they contain blocks of central pigment or sporulating bodies (usually found only in internal organs) or more rarely, the unmistakable crescents.

While positively demonstrated malarial parasites always indicate malaria, what of successive negative findings? Osler found plasmodia in 531 cases, yet Baccelli estimates the negative findings in malaria at 2 3-10 per cent. Indeed, in some of Osler's fatal cases reported by Barker, it seems that plasmodia were not found. The time of examination, the previous administration of quinine, the skill of the clinician, the acuteness or chronicity of the infection, etc., influences the results. As a rule it is well to doubt a diagnosis of malaria when we repeatedly fail to find the plasmodia, in fresh specimens, uncontaminated by protoplasmic poisons, as methyl blue, which alter or kill the blood. Sometimes the quinine test clears the case. As exceptions may be mentioned pernicious cases observed by Celli, Bignami, and Marchiafava in which pernicious symptoms as hyperpyreria, coma, grave anaemia and delirium persisted after the plasmodia disappeared from the peripherae blood and the autopsy found few parasites in the internal organs, though much detritus, pigment, anaemia, necroses in the liver, etc., capillary hemorrhages and alterations in the endothelial lining of the cerebral capillaries. Other cases of rapid death with few parasites in the blood and viscera are considered instances of malaria with sunstroke.

Two. Splenic Puncture is not justifiable, since death may result.

Three. A diagnosis from symptoms alone as paroxysm, spleen, fever curve, herpes, etc., is impossible. Absolute diagnosis is demonstration of the plasmodium.

Four. A diagnosis from success of a quinine therapy amounts to a probability only. Some few virulent cases resist the drug and conversely all is not malaria which responds to quinine. In doubtful cases this is a good and urgent method of diagnosis, but relief should be almost immediate to establish any logical connection between symtoms and cure.

Differentiation.

From typhoid. Without blood examination malaria and typhoid may be confused—very rarely do they co-exist. Malaria benign or malign may resemble typhoid closely, with roseolae, slow dierotic pulse, splenic tumor, headache, fever curve, cerebral and abdominal symptoms, intestinal hemorrhage, etc., etc., and again typhoid with remittent temperature may simulate malaria.

In typhoid-like malaria, the temperature offers no certain diagnostic criterion, yet a temperature which obeys no law, vomiting, tender liver and epigastrium, irregularly disposed bronchitis, pulmonary congestions shifting and variable, pulsating and neuralgic headaches, marked anaemia and melanaemia, usually a ready break in the symptoms after quinine thereupon and the plasmodium in the blood establish the diagnosis. The Widal test may be absent in typhoid, hence the necessary cautiousness in excluding typhoid on this ground alone.

Icterus, haemoglobinuria, leucocytosis, pronounced, indeed, pernicious anaemia, speak for malaria.

The bilious type may resemble yellow fever or the acute febrile jaundice of Weil, the haemorrhagic type may present the exact picture of Werlhoff's disease and the irregular intermittent can closely simulate cryptogenetic sephcaemia or cholecptitis, hectic phthisis, Malta fever, filarial disease, sudocarditis, influenza, the fever of malignant new growths, especially Sarcomata or organic nervous changes. The subject of treatment falls to the care of Dr. Favill, and its object is to secure the certain absorption of quinine and constantly maintain it in solution in the blood against the time of susceptible sporulation of the plasmodium malariae.

THE CRESCENT FORM OF THE MALARIAL PARASITE.

By Robert B. Preble, M. D., Chicaoo.

*In 1896 I read a paper before this society upon malaria as seen in Chicago, and expressed the opinion that the aestivo-autumnal malaria was not acquired in Chicago, basing this opinion on blood examination of several hundred cases, among which I found no case of the aestivo-autumnal fever acquired here. A short time after this I found a case of spring and autumn fever undoubtedly acquired in the city, and since then I have seen a few others. This seemed a very peculiar

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